

REMARKS

Amendments in the claims

Following entry of the amendment requested herein, Claims 28-36, 38-41, 45-48, 52-56 are pending. Of the pending Claims, Claims 38-40, 45-48, 52-56 are withdrawn. Claims 1-27, 37, 42-44, 49-51 and 57-59 were cancelled previously.

Claim 28 is amended herein to remove the process limitation.

Claim 30 is amended herein to correct antecedent basis.

No new matter is added, and no change in inventorship is believed to occur, as a result of any amendment herein.

RESPONSE TO OFFICE ACTION DATED 21 JULY 2010

1. Rejection under 35 U.S.C. §103(a) – Ulman in view of Mueller

Claims 28-32, 34-36, and 41 remain rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over U.S. Patent No. 5,658,975 (“Ulman”) in view of U.S. Patent No. 6,620,429 (“Mueller”). The rejection is respectfully traversed. At the outset, Applicant submits the present After-Final Response to place the claims in better condition for appeal or for allowance.

Claim 28, as amended herein, recites:

A transdermal therapeutic system comprising a drug-containing adhesive matrix, wherein the drug-containing adhesive matrix comprises:
rotigotine free-base and
hot-meltable adhesive,
wherein the drug-containing adhesive matrix exhibits at 160°C a
dynamic viscosity of not more than 100 Pa·s.

I. No Motivation to Combine Ulman and Mueller

The Examiner’s asserted obviousness rationale is based on Ulman and Mueller.

Ulman reports a generic hot-melt TTS.

Mueller reports a solvent-based rotigotine TTS, but not a hot-melt TTS.

The Examiner’s asserted obviousness rationale is limited to one sentence in the 10-page Office Action, and is stated as follows:

“One of ordinary skill in the art at the time of the invention was made would have been motivated to make such a composition [rotigotine TTS]

because the amount of drug released from the transdermal formulation can be increased or controlled, as explained by Ulman.” (21 July 2010 Office Action, pg. 5, emphasis added)

Applicant respectfully maintains all arguments already made of record, and that there is no KSR-based motivation to combine Ulman and Mueller. The Examiner’s asserted motivation to determine obviousness is wholly-deficient in establishing a presumption of *prima facie* obviousness for at least the following reasons:

1. **Ulman’s utility teaches away from rotigotine:** The Examiner’s rationale: “[T]he amount of drug released from the transdermal formulation can be increased or controlled” from Ulman is in direct relation to Ulman’s express utility to “increase” hydrophilic drugs. Rotigotine is not a hydrophilic drug, but a lipophilic drug. Therefore, on its face, the asserted rationale: “[T]he amount of drug released from the transdermal formulation can be increased or controlled”, can not be motivation to put rotigotine free-base into Ulman’s hydrophilic hot-melt TTS.
2. **Ulman must be read “as a whole”:** Applicant respectfully reminds the Office, that a prior art reference must be read as a whole. When Ulman is properly viewed “as a whole”, one can not ignore Ulman’s express and exclusive emphasis on hydrophilic drugs.
 - a. Ulman starts out discussing the prior art “These hot-melt compositions have been found to be inadequate for the delivery of **hydrophilic** drugs...” (Col 1, lines 61-62)
 - b. “There are several advantages to having a hot-melt composition that is **hydrophilic**.” (Col 1, lines 63-64)
 - c. “One advantage is that higher dosages of **hydrophilic** drugs can be employed without destroying the pressure sensitive adhesive.” (Col 1, lines 64-67)
 - d. “It is an object of this invention to provide a hot-melt silicone pressure sensitive adhesive composition that has improved **hydrophilic** characteristics while maintaining the pressure sensitive adhesive properties of shear, adhesion and release.” (Col 2, lines 3-7)

- e. “It is generally recognized by one skilled in the art that the presence of polypropylene oxide groups can be detrimental to the **hydrophilicity**...” (Col 5, lines 39-41)
 - f. “One of skill in the art will be able to readily determine the amount of polypropylene oxide that can be present without losing the **hydrophilic** characteristics of the wax. (Col 5, lines 43-46)
 - g. “Due to the presence of the siloxylated polyether waxes in the hot-melt silicone pressure sensitive adhesive composition of the instant invention, the resulting adhesives have improved **hydrophilic** characteristics, thus allowing quicker delivery of drugs that are **hydrophilic** in nature” (Ulman, Col 7, lines 37-41).
3. **No reasonable guidance:** Ulman provides no teaching or suggestion that rotigotine free-base could be used in a hot-melt TTS. Ulman is completely generic. Ulman contains no examples with any active agents, and does not even mention one specific active agent in the specification. Just because Ulman asserts that some amount of unnamed “bioagent” can be increased (or controlled) in their hot-melt TTS, provides no reasonable motivation that, specifically rotigotine free-base (a lipophilic drug) could be used in an Ulman hot-melt TTS, especially since it was believed that rotigotine could not be used at “hot” temperatures because it would degrade. It is simply incredible to contemplate that an ordinary artisan would believe that Ulman stood for the proposition that any drug could be used in Ulman’s hot-melt TTS, and especially a lipophilic drug like rotigotine free-base.
4. **Ulman is a vacuum of information:** The Examiner is relying on a vacuum of information instead of what is expressly being taught in Ulman. The Examiner maintains that Ulman does not prohibit use of lipophilic drugs. This is irrelevant because it is useless as a positive teaching toward selection of a rotigotine free-base hot-melt TTS. The relevant question is where is the motivation to take a lipophilic drug, which degrades at high temperature, from a solvent-based system

(Mueller) and put it in a hot-melt system where it could degrade? Applicant submits that no such motivation exists, and certainly not within Ulman or Mueller.

- 5. Ulman does not teach rotigotine hot-melt TTS:** How can “Ulman clearly teach[es] use of the disclosed hot-melt composition for transdermal drug delivery”. (21 July 2010 Office Action, pg. 4, lines 3-4) when, to the contrary, nowhere does Ulman teach a rotigotine free-base hot-melt composition:
- a. Rotigotine is not mentioned;
 - b. Ulman mentions no other drugs, even drugs like rotigotine; and
 - c. Ulman’s express teaching is for hydrophilic drugs.

II. Surprising and Unexpected Results

Regardless of whether there was motivation to combine Ulman and Mueller, and arrive at Applicant’s invention, the Examiner has not responded to Applicant’s argument presented in the May 2010 response, as follows:

- At the time of the invention, rotigotine was known to be susceptible to oxidation. Therefore, it was surprising to find that rotigotine remains stable even when heated to temperatures around 160°C.
- Even though rotigotine tends to decompose in an oxidative fashion, it is surprisingly stable in a hot-melt adhesive.
- This constitutes factually strong evidence that no one of ordinary skill could have predicted that rotigotine could be used in a hot-melt TTS.
- **If rotigotine decomposes at high temperatures, than how could one know it would work in a hot-melt TTS?**

Therefore, a presumption of *prima facie* obviousness does not exist over Ulman and Mueller. Applicant respectfully requests withdrawal of the present rejection.

2. Rejection under 35 U.S.C. §103(a) – Ulman in view of Mueller & Noel

Applicant incorporates by reference the argument presented in their 13 May 2010 response.

3. Provisional obviousness-type double patenting

Applicant incorporates by reference the argument presented in their 13 May 2010 response.

4. Conclusion

It is believed that all of the stated grounds of rejection are properly traversed, accommodated, or rendered moot herein. Applicant therefore respectfully requests that the Examiner reconsider and withdraw all presently outstanding rejections. It is believed that a full and complete response has been made to the present Action and that the application is in condition for allowance.

Should any issues remain, the Examiner is invited to call the undersigned at the telephone number given below.

Respectfully submitted,
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